UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/054,562	01/22/2002	Ramaswamy Chandrashekar	HW-8-2	9225

7590 04/22/2003

Heska Corporation
1613 Prospect Parkway
Fort Collins, CO 80525

EXAMINER
BASKAR, PADMAVATHI

ART UNIT	PAPER NUMBER
1645	9

DATE MAILED: 04/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/054,562	Applicant(s) CHANDRASHEKAR ET AL.	
	Examiner Padmavathi v Baskar	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-24 and 27-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24 and 27-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment filed on 3/17/03 (Paper No: 8) is acknowledged. Claims 25, 26 and 32-36 have been canceled. Claims 21-24 and 27- 31 have been amended. Claims 21-24 and 27- 31are pending in the application.

Election

2. Applicant's election of Group 1, Claims 21-24, 27-31 in Paper No. 8 **without traverse** is acknowledged. Applicant requests the Office to examine Claims 21-24, 27-31 with respect to SEQ.ID.NO: 1-5 in this application and the examiner is examining the claims with respect to SEQ.ID.NO: 1-5 as all these sequences are structurally related.

Claim Rejections - 35 U. S. C. 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 21-24 and 27-31 are rejected under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published June 15, 1998 in the Federal Register at Volume 63, Number 114, pp 32639-32645 (also available at www.uspto.gov). This is a written description rejection.

The claims are drawn to an isolated Dirofilaria immitis protein or a composition comprising the same, wherein said protein is encoded by a nucleic acid molecule that hybridizes to a nucleic acid sequence of SEQ.ID.NO: 2 and 5, said protein comprises an amino acid sequence that is at least 95% identical to SEQ.ID.NO: 4 (the examiner is considering the protein encoded by the nucleic acid sequences SEQ.ID.NO: 2 and 5 as hybridizing variants and amino acid sequence 95% identical to SEQ.ID.NO: 4 as a variant).

The specification describes as part of the invention, an isolated protein of SEQ ID NO: 4, which is a Dirofilaria cuticlin protein. The specification teaches translation of SEQ ID NO: 1, the coding strand of nucleic acid molecule nDiCut-1A, yields an essentially full length parasitic helminth cuticlin protein of 387 amino acids, referred to herein as PDiCut-1A, the amino acid sequence of which is represented by SEQ ID NO: 4. The open reading frame spans from nucleotide 167 through nucleotide 1327 of SEQ ID NO: 1 and a termination (stop) codon spans from nucleotide 1329 through nucleotide 1331 of SEQ ID NO: 1. The coding region encoding PDiCut-1A, is represented by SEQ ID NO: 3 (the coding strand). However, the specification does not teach (1) an isolated Dirofilaria immitis protein or a composition comprising hybridizing variants to either or any of SEQ ID NO 2 and 5 (2) a protein or a composition comprising an amino acid sequence that is at least 95% identical to SEQ.ID.NO: 4.

The actual biological function of a protein comprising 95% of homology with SEQ ID NO: 4 or hybridizing variants to either or any of SEQ ID NO 2 and 5 is not set forth in this specification. USPQ2d 1111 makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116).

Therefore, an isolated Dirofilaria immitis protein or a composition comprising an amino acid sequence of SEQ.ID.NO: 4 meets the written description provision of 35 U.S.C. 112, first paragraph for the reasons set forth below.

The specification fails to teach a protein sequence of 95% of homology with SEQ ID NO: 4 or hybridizing variants to either or any of SEQ ID NO 2 and 5. It is noted that the claimed variants do not exist as an invention independent of their function in encoding a protein of SEQ.ID.NO: 4. Further, the specification lacks support for a protein that is encoded by hybridizing variants to either or any of SEQ ID NO 2 and 5 or variant of SEQ.ID.NO: 4. The actual structure or other relevant identifying characteristics of each protein (i.e. homolog) having the claimed properties of the cuticlin protein can only be determined empirically by actually making every nucleic acid that encodes the recited variability (i.e. the instant 95% identity) and testing each to determine whether such a protein having the particularly disclosed properties of an helminth cuticlin protein comprising an amino acid sequence SEQ ID NO: 4. For example, if there is a well-established correlation between structure and function in the art, one skilled in the art will be able to reasonable predict the complete structure of the claimed invention from its function. Thus there is no written description support for proteins or compositions as claimed.

Applicants propose that the skilled artisan is to modify a known nucleic acid sequence encoding a known protein sequence and that modification would still describe applicant's invention as a protein comprising an amino acid sequence SEQ ID NO: 4 as disclosed. The protein has specific biological properties dictated by the structure of the protein and the corresponding structure of the structural gene sequence which encodes it. There must be some nexus between the structure of a gene sequence and the structure of the protein encoded, and the function of that encoded protein. However, similar function cannot be predicted from the modification of the structure of the polynucleic acid sequences of SEQ.ID.NO: 2, SEQ.ID.NO 5,

and amino acid sequence of SEQ.ID.NO: 4 because these proteins have not been described by the specification, nor would they be structurally related to SEQ.ID.NO: 4. Adequate written description requires more than a mere statement that it is part of the invention. See Fires v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chuaai Pharmaceutical Co Ltd., 18 U5PQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 U5PQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Applicants have not described a genus of proteins that hybridize as claimed or 95% identical as claimed.

5. Claims 21-24 and 27-31 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling an isolated Dirofilaria immitis protein or a composition comprising said protein, wherein said protein is encoded by SEQ.ID.NO: 1 and SEQ.ID.NO: 3, said protein or a composition comprising an amino acid sequence SEQ.ID.NO: 4, does not reasonably provide enablement for an isolated Dirofilaria immitis protein or a composition comprising hybridizing variants to either or any of SEQ ID NO 2 and 5 and a protein or a composition comprising an amino acid sequence that is at least 95% identical to SEQ.ID.NO: 4 (the examiner is considering this as a variant of SEQ.ID.NO: 4). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches nucleic acid (SEQ ID N0: 3) encoding a D.immitis protein of SEQ ID N0: 4 from D.immitis. The specification is not enabled for the claimed protein or composition comprising hybridizing variants to either or any of SEQ ID NO 2 and 5 and variant of SEQ.ID.NO: 4 with similar structure because: 1) the specification fails to teach where variation of SEQ ID N0: 4 is permitted such that the protein is still able to function as a composition for inhibiting or curing or diagnosing parasitic infections; 2) the specification lacks

any written description of any variant of D.immitis or Dirofilaria nematode species homologs of SEQ ID N0: 4 which are capable of similarly functioning; 3) the specification fails to teach how to use protein sequences which are variant of SEQ ID N0:4 in diagnosis/detection because the specification fails to teach what are the critical nucleic acid residues that can be modified and still achieve a nucleic acid that will function to produce a protein that has vaccine or diagnostic function as asserted in the specification; and 4) the art teaches that even replacement of a single amino acid residue may lead to both structural and functional changes in biological activity and immunological recognition of a protein. As to points 1)- 4), the specification fails to provide a written description of any protein variant (95% variant) and any protein encoded by the nucleotide sequence of SEQ ID N0: 1 and 5, which function equivalently. The specification fails to teach the critical protein residues involved in any function of the protein encoded by SEQ ID N0: 4 such that the skilled artisan is provided no guidance to test, screen or make the plethora of nucleic acid sequence variants of SEQ ID N0: 2 and 5 of a claimed protein of no defined structure, even using conventional technology which allow for a screening process. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence identity or hybridization results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function and therefore lacks support regarding enablement. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecule of related function upon a significant amount of further research. One of skill in the art would be reduced to merely randomly altering nucleic acids which would lead to

unpredictable results regarding the functional activity of the protein or its relationship to SEQ.ID.NO: 4. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted a priori and must be determined empirically on a case by case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol. 1991, 5(7): 1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which products proteins that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition. The specification has not taught which residues of the nucleotide sequence of SEQ ID N0: 2 and 5 and amino acid sequences of SEQ.ID.NO: 4 can be varied and still achieve a protein that is functional as

claimed. Further, random insertions, deletions and changes to a nucleotide sequence do not provide guidance to make a related protein. Therefore, the claimed isolated protein results in an unpredictable biomolecule without any function. Therefore, lacks support regarding enablement.

6. No claims are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 A.M. to 4:00 P.M. EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909 The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

4/14/03

Patricia A. Duffy
PATRICIA A. DUFFY
PRIMARY EXAMINER